TITLE: **Diminution of the anti-PRP response to a combined DTaP/Hib vaccine by concurrent inactivated poliovirus vaccination**

INVESTIGATORS: Margaret Rennels, Janet Englund, David Bernstein, Genevieve Losonsky, Edwin Anderson, Michael Pichichero, Flor Munoz, Mark Wolff

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BACKGROUND: In pre-licensure immunogenicity studies of Hib and DTaP vaccines concurrent OPV was administered. We therefore conducted a trial in which children received at 2, 4, and 6 months of age DTaP and Hib vaccine (separately or combined) either with all OPV, all IPV, or sequential IPV-OPV. This study was conducted when all 3 poliovirus vaccine schedules were considered acceptable.

METHODS:
Subjects: Healthy infants between 6 – 12 weeks of age were recruited through 5 NIH Vaccine Evaluation Units.
Vaccines: The DTaP (Tripedia), Hib (ActHIB) and combined DTaP/Hib (TriHIBIT) and IPV vaccines were manufactured and donated by Pasteur Merieux Connaught (now Adventis Pasteur). OPV was manufactured by Wyeth-Lederle Vaccines.
Design:

Group	2 months	4 months	6 months
A	OPV + DTaP + PRP-T	OPV + DTaP + PRP-T	OPV+ DTaP + PRP-T
B	OPV + DTaP / PRP-T	OPV + DTaP / PRP-T	OPV + DTaP / PRP-T
C	IPV + DTaP / PRP-T	IPV + DTaP / PRP-T	OPV + DTaP / PRP-T
D	IPV + DTaP / PRP-T	IPV + DTaP / PRP-T	IPV + DTaP / PRP-T

(+ = separate anatomic site; / = combined in same syringe)

Serology: At FDA's request, anti-PRP concentrations were measured at Connaught laboratories by RIA.

RESULTS:
Immunogenicity, primary series:
The major, and unexpected, finding was a significant diminution in the anti-PRP concentrations in children given 2 or 3 doses of IPV concurrently with DTaP/PRP-T compared to those given OPV and either separately administered DTaP and PRP-T, or combined DTaP/PRP-T. There were no significant differences between the per protocol and intent to treat results. Post dose 3 per protocol antibody responses to PRP were:

Group	N	%≥.15	%≥1.0	GMC (95% CI)
A	112	98	81	4.43 (3.34-5.88)
B	125	94	78	3.17 (2.34-4.29)
C	118	86	58	1.33 (0.93-1.89)
D	118	84	53	1.21 (0.87-1.69)

The P values for the following pairwise comparisons of GMCs, % ≥.15, and %≥1.0 were all 0.0001: A vs. C; A vs. D; B vs. C; B vs. D. There were no significant differences in the antibody responses to PRP-T between children who were given all OPV with either separately administered DTaP and PRP-T (A) or DTaP /PRP-T (B).

Immunogenicity, booster dose:

Forty-seven children had a post-dose 3 anti-PRP concentration less than 0.15 : g/ml. Forty-three of these children were located; all had received a 4th dose of a PRP containing vaccine. A post-dose 4 blood specimen was obtained between 4 and 35 weeks after this booster dose. Fifteen of these children (35%) had <1.0 µg/ml of anti-PRP antibody; the distribution of these 15 children by treatment group was A-1, B – 2, C-9, and D-3. Six of the 43 (14%) also had less than 0.15 : g/ml (A-1, B-1, C-2, D-2). The significance of these data is unclear because of the variable and often lengthy interval between vaccination and blood sampling.

CONCLUSION: In this trial, concurrent IPV appeared to interfere with the anti-PRP response to this lot of this DTaP/Hib vaccine.